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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,281	10/30/2003	Paul K. Wolber	10030355-1	3574

22878 7590 12/22/2006

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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/22/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,281	WOLBER ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 6 October 2006 in which claims 1 and 21 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The Interview Summary is acknowledged and the interview record is complete.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of Applicant's arguments on page 7 of the Remarks.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-13 and 21-25 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 21-25 rejected under 35 U.S.C. 102(b) as being anticipated by McGall (U.S. Patent No. 5,843,655, issued 1 December 1998).

Regarding claim 21, McGall teaches a method of detecting the presence of a nucleic acid analyte in a sample, said method comprising contacting a nucleic acid array, said array comprising a set of two or more nucleic acid depurination features each having a depurination probe and having a nucleic acid ligand that specifically binds to said nucleic acid analyte with a sample suspected of having said analyte;

namely, McGall teaches a nucleic acid array produced photolithographically and having oligonucleotides thereon (Figure 8), wherein R1 and R2 are the depurination features. R1 and R2 each have a depurination probe and a nucleic acid ligand; namely, those oligonucleotides marked with a "D" are depurination probes and the remaining oligonucleotides are nucleic acid ligands (column 9, lines 22-38). McGall teaches the array is treated with a sample of suspected of comprising said nucleic acid analyte under conditions for binding of said analyte to said nucleic acid ligand on said array to occur (column 13, lines 33-52). McGall also teaches detecting the presence of binding complexes on the surface of said array to detect the presence of said nucleic acid analyte in said sample; namely, a CCD imaging system is used to detect hybridization (column 13, lines 33-52).

Regarding claim 22, McGall teaches the method of claim 21, wherein said sample comprises a collection of labeled target nucleic acids that specifically bind to said nucleic acid depurination features (column 13, lines 33-52).

Regarding claim 23, McGall teaches the method of claim 21 further comprising transmitting a result from a reading of an array according to the method of claim 21 from a first location (e.g., the surface of the array) to a second location (e.g., a line scanner; column 12, lines 56-67).

Regarding claim 24, McGall teaches the method of claim 23 further comprising the second location is a remote location; namely, a line scanner (column 12, lines 56-67), which is remote from the surface of the array.

Regarding claim 25, McGall teaches the method of claim 21 further comprising receiving a transmitted result of a reading of an array obtained from the method of claim 21; namely, the transmitted images are stored in a computer (column 12, lines 56-67).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over by McGall (U.S. Patent No. 5,843,655, issued 1 December 1998) in view of Weng et al (U.S. Patent No 6,691,042 B2, issued 10 February 2004).

Regarding claim 1, McGall teaches a method of detecting the presence of depurination reaction products on a surface of an in situ produced nucleic acid array, said method comprising contacting an in situ produced nucleic acid array, said array including at least one depurination probe feature having a depurination probe with a sample suspected of having said analyte; namely, McGall teaches a nucleic acid array produced photolithographically (i.e., in situ) and having oligonucleotides thereon (Figure 8), wherein R1 and R2 are the depurination features. R1 and R2 each have a depurination probe; namely, those oligonucleotides marked with a "D" are depurination probes in the feature (column 9, lines 22-38).

McGall teaches that the two areas of the array are exposed to a test condition to test for depurination at the depurination sites D (Figure 8 and column 9, lines 39-49). McGall also teaches that the test condition is followed by exposure to conditions that cleave depurinated sites (column 9, lines 50-60) and subsequent detection of the remaining label from the uncleaved oligonucleotides of the array (column 9, lines 61-67). The detection of the remaining uncleaved oligonucleotides determines the presence of depurination reaction products on the array by comparison of the first cleaved area to the other (i.e., second) area of the array, which is subjected to the same test conditions but not the cleavage conditions (column 9, lines 61-67); thus, the second area retains all of the oligonucleotides originally present, whereas the cleaved area has lost all of the depurinated oligonucleotides.

While McGall also teaches subjecting the arrays to test conditions, wherein test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57), McGall does not explicitly show hybridization as a test condition for determining depurination.

However, Weng et al teach a method of detecting the presence of nucleic acids; namely, measuring expression levels of nucleic acids using microarrays (column 8, lines 60-67). Weng et al also teach hybridization is used as a test condition (column 4, lines 58-67), and that hybridization as a test condition has the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

Use of the hybridization test condition of Weng et al in the method of McGall is thus interpreted as outlined in the single exemplary embodiment: two ensembles of oligonucleotides in two areas of an array of McGall are both subjected to the same hybridization test condition of Weng et al. The ensemble in the first area is subjected to cleavage of depurination products. The amount of label at each site is detected and compared to determine the presence of depurination reaction products on the surface of the array. Thus, the resultant binding complexes of the uncleaved depurination probes are compared to the

cleaved depurination probes to determine the presence of depurination reaction products on the surface of the array.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall using hybridization as a test condition as taught by Weng et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing a method of controlling the quality of the microarray production process as explicitly taught by Weng et al (column 5, lines 29-32).

Regarding claim 2, the method of claim 1 is discussed above. McGall also teaches that the method detects the amount of depurination products on said surface; namely, the amount of label in an area is determined after cleavage of the depurinated oligonucleotides (column 2, lines 48-50).

Regarding claim 3, the method of claim 2 is discussed above. McGall also teaches the detection of a relative amount (column 7, lines 63-67).

Regarding claim 4, the method of claim 2 is discussed above. McGall also teaches the labeling of the target nucleic acid (column 11, lines 55-56).

Regarding claim 5, the method of claim 4 is discussed above. McGall also teaches fluorescent labels and signals (column 3, lines 24-31).

Regarding claim 6, the method of claim 5 is discussed above. McGall also teaches a fluorescent signal having an intensity inversely proportional to the amount of depurination products present (column 9, lines 65-67).

Regarding claim 7, the method of claim 1 is discussed above. McGall also teaches an array including two or more different depurination probe features each corresponding to a distinct depurination probe; namely, the array has a plurality of areas R1 and R2 (Figure 8), each having depurinated nucleic acids thereon.

Regarding claim 8, the method of claim 1 is discussed above. McGall also teaches early and late depurination probe features; namely, the depurination features occur at positions in the sequence relative to the surface (Figures 8 and 9).

Regarding claim 9, the method of claim 1 is discussed above. McGall also teaches arrays including two or more features whose synthesis was started at different times; namely, areas on the surface are sequentially synthesized (column 9, lines 30-35).

Regarding claim 10, the method of claim 1 is discussed above. McGall also teaches a known deblock dose; namely, selective deprotection and coupling cycles are repeated until the desired products are obtained (column 5, lines 2-25), the desired products requiring a known number of cycles.

Regarding claim 11, the method of claim 1 is discussed above. McGall also teaches the method further comprises evaluating the level of depurination that occurred during in situ fabrication of said array (column 2, lines 48-50).

Regarding claim 12, the method of claim 11 is discussed above. McGall also teaches the method is a method of evaluating the quality of an in situ nucleic acid array synthesis protocol (column 1, lines 7-9).

Regarding claim 13, the method of claim 12 is discussed above. McGall also teaches the method is employed to evaluate the quality of a plurality of nucleic acid arrays fabricated according to said protocol; namely, arrays in different test areas on the substrate are independently evaluated (column 9, lines 38-49).

Response to Arguments

7. Applicant's arguments filed 6 October 2006 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Regarding the rejection of claim 21 under 35 USC 102(b) as anticipated by McGall, Applicant argues on page 7-8 of the Remarks that McGall does not teach two or more depurination

features that include at least one depurination probe, and that none of the probes of McGall's array are used to directly detect depurination reaction products on the surface of the array.

However, McGall does teach an array comprising a set of two or more nucleic acid depurination features each having a depurination probe and having a nucleic acid ligand that specifically binds to said nucleic acid analyte with a sample suspected of having said analyte; namely, McGall teaches a nucleic acid array produced photolithographically and having oligonucleotides thereon (Figure 8), wherein R1 and R2 are the depurination features. R1 and R2 each have a depurination probe and a nucleic acid ligand; namely, those oligonucleotides marked with a "D" are depurination probes and the remaining oligonucleotides are nucleic acid ligands (column 9, lines 22-38). Page 16 of the specification defines depurination probes as "probes that have a known number of purine bases, and specifically Adenosine or A bases (lines 8-10)." Because the array of McGall is produced de novo by photolithographic synthesis, each sequence of the array is known in its entirety, including the number of purines and adenosines.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., direct detection of depurination products on the surface of the array) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 21 merely recites "two or more depurination features each having a depurination probe and having a nucleic acid ligand that specifically binds to said nucleic acid analyte" (lines 4-6 of claim 21). The claim is therefore broadly interpreted as requiring a nucleic acid ligand that binds to the analyte; namely, a nucleic acid probe (i.e., ligand) in addition to the depurination probe, wherein the additional non-depurinated probe binds to the analyte and is detection in the binding complexes of the analyte. Thus, in its current form, claim 21 has no method steps requiring the use of detection of the depurination probe; rather, the only requirement for the depurination probe is that it be present at each feature, which is taught by McGall as described above.

B. Regarding the rejection of claim 1 under 35 USC 103(a) as obvious of McGall in view of Weng, Applicant argues on pages 8-9 of the Remarks that McGall does not teach direct detection of depurination reaction products on the surface of the array; rather, as acknowledged by Applicant on pages 7-8 of the Remarks, McGall teaches detection of the remaining uncleaved oligonucleotides remaining on the array, while the depurinated probes are removed.

It is noted that Applicant's use of the term "direct detection" is not found in claims 1-13, and that claim 1 does not require detection of anything that has been cleaved; rather, claim 1 merely requires detection of binding complexes in a depurination probe feature to determine the presence of determination reaction products.

As noted above, McGall teaches two ensembles of oligonucleotides in two areas of an array of McGall are both subjected to the same test condition (column 9, lines 23-67). The ensemble in the first area is subjected to cleavage of depurination products. The amount of label at each site is detected and compared to determine the presence of depurination reaction products on the surface of the array. Thus, the uncleaved depurination probes of one area are compared to the cleaved depurination probes of another area to determine the presence of depurination reaction products on the surface of the array.

While McGall also teaches subjecting the arrays to test conditions, wherein test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57), McGall does not explicitly show hybridization as a test condition.

However, Weng et al teach a method of detecting the presence of nucleic acids; namely, measuring expression levels of nucleic acids using microarrays (column 8, lines 60-67). Weng et al also teach hybridization is used as a test condition (column 4, lines 58-67), and that hybridization as a test condition has the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

Thus, modification of the method of McGall et al with the teaching of hybridization as a test condition of Weng et al results in both of the two areas of the array of McGall et al having nucleic acids hybridized to the depurination probes. One area is then cleaved, and both areas are scanned to detect any label present. The binding complexes of the depurination probes in the uncleaved area are thus directly detected and compared to the cleaved complexes to determine the presence of depurination reaction products on the surface of the array. Thus, all of the limitations of independent claim 1 are obvious over the combined teachings of McGall and Weng et al.

Conclusion

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). 10. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

JULIET C. SWITZER
PRIMARY EXAMINER